UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,896	06/01/2000	WOLFGANG PIEPERSBERG	RDID0011US	6502

7590 08/30/2002

THE LAW OFFICE OF JILL L. WOODBURN, L.L.C.
6633 OLD STONEHOUSE DRIVE
NEWBURGH, IN 47630-1785

EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/30/2002 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/485,896	PIEPERSBERG ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-35* is/are pending in the application.

4a) Of the above claim(s) *15-17,26-30 and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,18-25,31 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 June 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

The request filed on 05/09/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/485,896 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 14-35 are pending in the application.

Claims 15-17, 26-30, and 32-34 and the subject matter of Groups II-IV as set forth in Paper No. 8 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Drawings

1. The drawings submitted with this application remain objected to by the Draftsperson. Refer to the "Notice of Draftsperson's Patent Drawing Review" attached to Paper No. 10 for details. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Specification/Informalities

2. The specification remains objected to as the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "PROCESS FOR THE PRODUCTION OF GDP-D-MANNOSE USING PHOSPHOMANNOMUTASE AND GDP-D-MANNOSE SYNTHASE ENZYMES". See MPEP § 606.01.

3. It is suggested that "Legends for the figures" at the middle of page 8 of the specification be replaced with, for example, "Brief Description of the Drawings".

Claim Objections

4. Claims 14 and 20 are objected to because the claims are drawn to non-elected subject matter. It is suggested that, for example, applicants amend the claims accordingly to remove non-elected subject matter from the claims.

5. Claim 21 is objected to because of the recitation of "E. coli" and "Corynebacterium sp.". Abbreviations should not be recited in the claims without at least once reciting the entire phrase, i.e., "Escherichia coli" and "Corynebacterium species" for which the abbreviation is used. Appropriate correction is required.

6. Claim 35 is objected to as being dependent upon non-elected claims 32-34.

Claim Rejections - 35 USC § 112, Second Paragraph

7. Claims 14, 18-25, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 14 (claims 21, 23, and 24 dependent therefrom), 18-20, 22, 25 are confusing in that it is not clear as to whether the process is practiced using a single polypeptide having multiple enzymatic activities, or if the claim is to be interpreted as a process using multiple polypeptides. The examiner has interpreted the claims as methods using a plurality of polypeptides. If the examiner's interpretation of these claims is incorrect, applicant should so state and clarify the record.

Claim Rejections - 35 USC § 112, First Paragraph

8. Claims 14, 18-21, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for the production of GDP-D-mannose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with GTP and D-mannose-6-phosphate as starting materials, does not reasonably provide enablement for a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose

synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 14 (claims 18-21 and 23-25 dependent therefrom) are so broad as to encompass a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of GDP-6-deoxyhexoses and precursors and secondary products of GDP-D-mannose broadly encompassed by the claims. In this case the disclosure is limited to a process for the production of GDP-D-mannose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with GTP and D-mannose-6-phosphate as starting materials.

The specification does not support the broad scope of the claims which encompass a process for the production of GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof because the specification does not establish a method for producing GDP-6-deoxyhexose using *any* precursors and secondary products of GDP-D-mannose using ManB and ManC as catalysts because it appears from Fig. 1 that *enzymes in addition to ManB and ManC are required for GDP-6-deoxyhexose synthesis* and in the event that ManB and ManC enzymes are sufficient for GDP-6-

deoxyhexose synthesis, it is unclear that these enzymes will have specificity for *any* precursors and secondary products of GDP-D-mannose.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

9. Claims 14, 18-23, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Elling et al. (Glycobiology 6:591-7, 1996; hereafter referred to as "Elling"). Claims 14, 18-23, and 31 are drawn to processes for the biosynthetic production of GDP-6-deoxyhexose or GDP-D-mannose using ManB and ManC enzymes as encompassed by the claims.

Elling teaches amplification of *Salmonella enterica* rfbK and rfbM genes encoding phosphomannomutase (EC 5.4.2.8) and GDP-α-D-mannose pyrophosphorylase (EC 2.7.7.13), respectively, cloning of said amplified genes into expression vectors, transforming *E. coli* with said vectors, expression of said enzymes (pages 591-2, under *Expression of phosphomannomutase and GDP-α-D-mannose pyrophosphorylase*), purification of said enzymes (pages 592, under *Enzyme purification*), and the use of said enzymes in the presence of D-mannose-6-phosphate and GTP (page 592, Fig. 1) for the batchwise production of GDP-α-D-mannose and isolation of the GDP-α-D-mannose by chromatographic and precipitation steps (page 592, under *Preparative synthesis and isolation of GDP-□-D-mannose*). This anticipates claims 14, 18-23, and 31 as written.

It is noted that applicants disclose in the specification at pages 2, 5, and 6 that phosphomannomutase is otherwise known as ManB and is encoded by the manB gene and GDP-mannose pyrophosphorylase is otherwise known as GDP-mannose synthase or ManC and is encoded by the manC gene. Therefore, the products of the rfbK and rfbM genes, i.e., phosphomannomutase and GDP-α-D-mannose pyrophosphorylase, respectively, are inherently the same as the ManB and ManC enzymes, respectively. The burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art. See *In re* Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re* Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

10. Claims 24, 25, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elling in view of Kragl et al. (US Patent 5,071,750; hereafter referred to as "Kragl"). Claims 24, 25, and 35 are drawn to a process for the biosynthetic production of GDP-6-deoxyhexose or GDP-D-mannose using cloned ManB and ManC enzymes, wherein: 1) the process is carried out continuously in an enzyme-membrane reactor (EMR) as encompassed by claim 24, 2) the enzyme is immobilized to a solid support and a buffer containing the substrates is percolated thereover (claim 25), or 3) the enzyme is immobilized on a solid support (claim 35).

Elling discloses the teachings described above. Elling does not teach practicing their method continuously in an enzyme-membrane reactor, using an immobilized enzyme with or without a buffer containing the substrate percolated thereover.

Kragl teaches the use of immobilized enzymes covalently coupled to a solid support for continuous enzymatic production of product. Kragl teaches the use of an EMR for continuous enzymatic biosynthesis, wherein the enzymes are retained by an ultrafiltration membrane which is located in front of the reactor outlet having an appropriate cut-off (column 3, lines 54-60). Kragl teaches that the advantage of using immobilized enzymes or EMR for biosynthesis is the facilitation of product isolation (column 4, lines 1 and 2).

Therefore, it would have been obvious to one of ordinary skill in the art to practice the method of Elling using immobilized enzymes or an EMR as taught by Kragl for the biosynthetic production of GDP-D-mannose. One would have been motivated to practice the method of Elling using immobilized enzymes or an EMR as taught by Kragl for the biosynthetic production of GDP-D-mannose in order to facilitate product isolation as described above. One would have a reasonable expectation of success for practicing the method of Elling using immobilized enzymes or an EMR as taught by Kragl for the biosynthetic production of GDP-D-mannose because of the results of Elling and Kragl. Therefore, claims 24, 25, and 35, drawn to a process for the biosynthetic production of GDP-6-deoxyhexose or GDP-D-mannose using cloned ManB and ManC enzymes, wherein: 1) the process is carried out continuously in an enzyme-membrane reactor (EMR) as encompassed by claim 24, 2) the enzyme is immobilized to a solid support and a buffer containing the substrates is percolated thereover (claim 25), or 3) the enzyme is immobilized on a solid support (claim 35) would have been obvious to one of ordinary skill in the art.

Conclusion

11. No claim is in condition for allowance. All claims are rejected.

All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600